In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: February 28, 2020

LORI L. SWEENEY, *Personal Representative of the Estate of* LUELLA A. GARLANGER,	*	No. 13-392V
Petitioner,	*	Special Master Sanders
v.	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	Influenza ("flu") Vaccine; Guillain-Barré Syndrome ("GBS"); Paraneoplastic Syndrome; Small Cell Lung Carcinoma
Respondent.	*	

Theodore J. Hong, Maglio, Christopher & Toale, Seattle, WA, for Petitioner.
Lara Englund, United States Department of Justice, Washington, DC, for Respondent.

DECISION[1]

On June 12, 2013, Lori L. Sweeney ("Petitioner"), in her capacity as the personal representative of the estate of Luella A. Garlanger ("Ms. Garlanger"), filed a petition for compensation under the National Vaccine Injury Compensation Program ("Vaccine Program" or "Program").[2] Petitioner alleged that the influenza ("flu") vaccine Ms. Garlanger received on October 15, 2011, caused her to develop Guillain-Barré syndrome ("GBS").[3] Pet. at 1–2, ECF No. 1.

After carefully analyzing and weighing all the evidence and testimony presented in this case in accordance with the applicable legal standards, I find that Petitioner has not met her legal

[1] This Decision shall be posted on the United States Court of Federal Claims' website, in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 note (2012) (Federal Management and Promotion of Electronic Government Services). **This means the Decision will be available to anyone with access to the Internet.** In accordance with Vaccine Rule 18(b), a party has 14 days to identify and move to delete medical or other information that satisfies the criteria in § 300aa-12(d)(4)(B). Further, consistent with the rule requirement, a motion for redaction must include a proposed redacted decision. If, upon review, the undersigned agrees that the identified material fits within the requirements of that provision, such material will be deleted from public access.

[2] National Childhood Vaccine Injury Act of 1986, 42 U.S.C. §§ 300aa-1 to -34.

[3] Guillain-Barré syndrome is a "rapidly progressive ascending motor neuron paralysis of unknown etiology, frequently seen after an enteric or respiratory infection." *Dorland's Illustrated Medical Dictionary* 1832 (32nd ed. 2012) [hereinafter "*Dorland's*"].

burden. Petitioner has failed to provide preponderant evidence that the flu vaccine Ms. Garlanger received on October 15, 2011, caused her to develop GBS. Accordingly, Petitioner is not entitled to compensation.

I. Procedural History

Petitioner filed her petition on June 12, 2013, Pet. at 1, and this case was assigned to former Special Master Hamilton-Fieldman, Notice of Assign., ECF No. 2. Over the next seven months, Petitioner filed ten exhibits in support of her petition. *See* Notice of Intent to File on CD, ECF No. 7; Pet'r's Ex. 10, ECF No. 9-1. Petitioner filed a statement of completion on January 23, 2014, ECF No. 10, and Special Master Hamilton-Fieldman ordered Petitioner to file an expert report by May 1, 2014, ECF No. 11.

Over the next year, Petitioner filed one additional exhibit, but four motions for extensions of time, ECF Nos. 14, 17, 19–20, which Special Master Hamilton-Fieldman granted, extending Petitioner's deadline to file an expert report to January 6, 2015, *see* Non-PDF orders, docketed May 5, 2014, July 2, 2014, Sept. 4, 2014; ECF No. 21. On January 6, 2015, Petitioner filed an expert report authored by Lawrence Steinman, M.D., along with fourteen pieces of supporting medical literature. Pet'r's Exs. 12–27, ECF Nos. 22-1–23-6. Special Master Hamilton-Fieldman ordered Respondent to file his Rule 4(c) report and an expert report by March 31, 2015. ECF No. 24.

After receiving one extension of time, Respondent filed his Rule 4(c) report and expert reports authored by Sara Vargas, M.D., and Eric Lancaster, M.D., and eighteen pieces of supporting medical literature on June 8, 2015. Resp't's Report, ECF No. 29; Resp't's Exs. A, C, ECF Nos. 30-1–30-2, 32-1; Resp't's Ex. A, Tabs 1–8, ECF Nos. 30-3–30-6, 31–1–31-4; Resp't's Ex. C, Tabs 1, 3–10, ECF Nos. 32-2–32-5, 33-1–33-7. Respondent filed an additional piece of supporting medical literature on June 12, 2015. Resp't's Ex. C, Tab 2, ECF No. 34-1. Special Master Hamilton-Fieldman ordered Petitioner to file a responsive expert report by July 27, 2015. Non-PDF order, docketed June 8, 2015.

Petitioner received one extension of time, ECF Nos. 35–36, and subsequently filed a supplemental expert report from Dr. Steinman and one piece of supporting medical literature on August 10, 2015, Pet'r's Exs. 28, 30, ECF Nos. 37-1, 37-3. Special Master Hamilton-Fieldman held a status conference with the parties on August 20, 2015, where they "discussed the expert reports recently filed by both [parties.]" *See* Min. Entry, docketed Aug. 20, 2019; ECF No. 38. Petitioner was ordered to file a supplemental expert report addressing concerns raised during the the status conference[4] by November 12, 2015. ECF No. 40 at 1.

Petitioner received one extension of time, ECF Nos. 42–43, and filed a supplemental expert report authored by Dr. Steinman on November 25, 2015, Pet'r's Ex. 32, ECF No. 44-1. Special

[4] Specifically, Special Master Hamilton-Fieldman ordered Petitioner to address "the vulnerability of the [Ms. Garlanger]'s immune system, the right sided development of neurological symptoms in relation to the development of cancer in her right lung, the size of the cancerous lesion when discovered in relation to the alleged injury, and the relevance of the [Ms. Garlanger]'s pre-existing conditions and history of smoking to causation." ECF No. 40 at 1.

Master Hamilton-Fieldman ordered Respondent to file a responsive supplemental expert report by January 20, 2016. Non-PDF Order, docketed Nov. 25, 2015. This case was reassigned to Special Master Roth on January 15, 2016. *See* Notice of Reassign., ECF No. 46. Respondent filed expert reports from Drs. Lancaster and Vargas on January 19, 2016. Resp't's Exs. E–F, ECF Nos. 47-1, 47-4.

Special Master Roth held a status conference with the parties on March 8, 2016, *see* Min. Entry, docketed Mar. 8, 2016, and ordered Petitioner to file an expert report from a radiologist by May 9, 2016, ECF No. 48. After receiving one extension of time, ECF No. 49, Non-PDF Order, docketed May 6, 2016, Petitioner filed an expert report from Gregory Arov, D.O., on June 8, 2016, Pet'r's Ex. 33, ECF No. 50-1. Special Master Roth held a status conference with the parties on August 29, 2016, during which they discussed Dr. Arov's report, noting that it "seem[ed] to support [R]espondent's position." *See* Min. Entry, docketed Aug. 29, 2016; ECF No. 51. Petitioner requested an opportunity to have Dr. Steinman review Dr. Arov's report and possibly submit a supplement report. ECF No. 51. Petitioner filed a supplemental expert report by Dr. Steinman on November 30, 2016. Pet'r's Ex. 36, ECF No. 54-1.

The parties convened for a status conference on April 27, 2017, *see* Min. Entry, docketed Apr. 27, 2017, and decided to proceed to an entitlement hearing, ECF No. 57. This case was reassigned to me on June 20, 2017. Notice of Reassignment, ECF No. 60.

Petitioner filed her opening pre-hearing brief on September 18, 2018. ECF No. 65. Respondent filed his responsive pre-hearing brief on October 18, 2018. ECF No. 66. Petitioner filed her reply pre-hearing submission on November 29, 2018. ECF No. 75.

On December 22, 2018, the appropriations act funding the Department of Justice ("DOJ") expired and appropriations for DOJ lapsed. *See* ECF No. 76. Citing this lapse, on January 4, 2019, Respondent filed a motion to stay the entitlement hearing. ECF No. 77. On the same day, I issued an order denying Respondent's motion. ECF No. 78.

On January 11, 2019, Petitioner filed a motion for leave to file additional pieces of medical literature out of time. ECF No. 79. I denied the motion on January 15, 2019, "because Petitioner could have filed [the] medical literature before the final prehearing submission deadline had passed and the inherent unfairness to Respondent that would result if [I] allowed Petitioner to file additional exhibits this close to trial during a government shutdown . . .." ECF No. 81.

I held the entitlement hearing on January 16, 2019. *See* Min. Entry, docketed Feb. 28, 2019. On February 28, 2019, I issued an order setting a schedule for the parties to submit post-hearing briefing. ECF No. 86. Petitioner filed her opening post-hearing brief on April 29, 2019. ECF No. 87. Respondent filed his responsive post-hearing brief, along with a supplemental expert report from Dr. Lancaster and three additional pieces of medical literature, on June 13, 2019. ECF No. 89; Resp't's Ex. H, ECF No. 90-1; Resp't's Ex. H, Tabs 1–3, ECF Nos. 90-2–90-4. Petitioner filed her reply post-hearing brief on June 27, 2019. ECF No. 91.

Neither party has filed any additional evidence, and this matter is now ripe for consideration.

II. Factual Background

Ms. Garlanger received the flu vaccination at issue in this case on October 15, 2011. Pet'r's Ex. 2 at 98. She presented to her primary care physician's ("PCP") office on November 1, 2011, complaining of "severe back [pain] at night, [and] right lower side [pain]" for the previous three days. *Id.* at 15. An exam of her spine revealed a paraspinous[5] muscle spasm on her right lumbar muscle but was otherwise normal. *Id.* at 16. She was prescribed Zanaflex[6] and Naprosyn[7] and directed to follow-up if her symptoms worsened. *Id.*

On November 4, 2011, Ms. Garlanger returned to her PCP with complaints of worsening pain and tingling. *Id.* at 13. The pain had spread to her entire back, but it was "on the ride side more than the left." *Id.* Her upper back pain began two days prior, and she had developed tingling in her right arm, although she did not state when this symptom began. *Id.* An examination was essentially unchanged from her last appointment. *Id.* at 14. She was prescribed Colace[8] and Hydrocodone-Acetaminophen and directed to go to the emergency room "if [she experienced] loss of sensation or weakness or worsening back pain." *Id.*

Ms. Garlanger had a follow-up with her PCP on November 7, 2011. *Id.* at 10. She reported that she was "[n]ot feeling any better" and noted that the "med[ications] help[ed] her to sleep, but during the day, [she had] no change [in her condition]." *Id.* An examination revealed normal strength and sensation, *id.* at 11, and she was assessed with a "[l]ikely pinched nerve[,]" *id.* at 12. She was referred to physical therapy ("PT"). *Id.*

On November 28, 2011, Ms. Garlanger returned to her PCP and stated that "she [could not] walk at all." *Id.* at 8. She reported that PT had "improved" her right-sided neck and lower back pain, "but over the last week, [she] ha[d] started to feel that her right side [was] weak" and "uncoordinated." *Id.* She now reported that she "cannot walk at all due to weakness and incoordination." *Id.* An examination revealed left-sided facial droop and decreased muscle strength and tone. *Id.* at 9. She was admitted to Lakeland Regional Medical Center that day because of a "suspect[ed] subacute CVA."[9] *Id.*

While admitted to the hospital, Ms. Garlanger underwent a stroke assessment, which was "negative," Pet'r's Ex. 7 at 835, as well as an MRI of her brain and a CT scan of her head, which

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[5] Paraspinal is defined as "near the spine" or "pertaining to a plane near the spine." *Dorland's* at 1381.

[6] Zanaflex is the "trademark for a preparation of tizanidine hydrochloride[,]" *Dorland's* at 2091, which is "an α_2-adrenergic agonist used as a short-acting agent to manage the increased muscle tone associated with spasticity, as that related to . . . spinal cord injury; administered orally[,]" *id.* at 1932.

[7] Naprosyn is the "trademark for a preparations of naproxen[,]" which is "a nonsteroidal anti[-]inflammatory drug that is . . . used in the treatment of pain[and] inflammation . . .; administered orally or rectally." *Dorland's* at 1232.

[8] Colace is the "trademark for a preparation of docusate sodium[,]" *Dorland's* at 382, which is "an anionic surfactant used as a stool softener, administered orally or rectally[,]" *id.* at 561.

[9] CVA is the acronym for "cerebrovascular accident." Neil M. Davis, MEDICAL ABBREVIATIONS: 26,000 CONVENIENCES AT THE EXPENSE OF COMMUNICATION AND SAFETY 105 (12th ed. 2005). A cerebrovascular accident is "an imprecise term for cerebral stroke." *Stedman's Medical Dictionary* 10 (28th ed. 2006).

were both "unremarkable," *id.* at 827. A workup revealed "positive ANA[10] . . . and SSA[11] antibod[ies] . . ." *Id.* at 827. On November 29, 2011, Ms. Garlanger underwent a lumbar puncture ("LP"),[12] which revealed elevated protein in her cerebrospinal fluid ("CSF")[13] at 129, with a reference range of 15–45. Pet'r's Ex. 7 at 961. It also revealed myelin basic protein in her CSF of 4.57, with a reference range of 0.0–1.10. Pet'r's Ex. 11 at 1571. On December 2, 2011, Ms. Garlanger saw Dr. Robert Ward, a neurologist. Pet'r's Ex. 3 at 20. His examination revealed decreased muscle strength in her extremities and "loss of pinprick, temperature and vibratory sensation . . .." *Id.* Dr. Ward conducted an electromyography ("EMG")[14] study, which he concluded was "consistent with an acute inflammatory demyelinating polyneuropathy" that he thought "may [have been] secondary to her vaccine exposure." *Id.* He recommended "treating [Ms. Garlanger] with IV IgG . . . for [five] days[,]" which she received during her hospital course. *Id.* at 4. Upon discharge on December 6, 2011, Ms. Garlanger's "[o]verall strength [had] very slowly improv[ed]," although "she [was] still very weak, [and] was unable to stand without maximum assist." Pet'r's Ex. 7 at 811. Her "[e]xtremities [were] still very uncoordinated and weak[,]" and she was "unable to empty her bladder . . .." *Id.* She was discharged to inpatient rehabilitation services at Lakeland Regional Medical Center. *Id.* at 1.

During her inpatient rehabilitation, Ms. Garlanger had a second assessment with Dr. Ward on January 6, 2012. Pet'r's Ex. 3 at 2. During her physical examination, Ms. Garlanger had "no sensation to pinprick, temperature or vibratory sensation distally in any of [her] limbs[,]" and had "no pinprick sensation in the lower extremities to the level of [her] pelvis." *Id.* at 18. The examination also revealed decreased strength in her extremities and "global muscle wasting." *Id.* Dr. Ward conducted a repeat EMG study. *Id.* at 2. His impression was "[d]emyelinating polyneuropathy with secondary axonal degeneration[,]" although he noted that there was "no evidence of ongoing acute denervation at [that] time." *Id.* Dr. Ward also noted that Ms. Garlanger was suffering "[m]arked debilitation secondary to" this finding. *Id.* He recommended subacute rehabilitation and discussed the possibility of obtaining a second opinion from a neuromuscular subspecialist. *Id.*

The family decided to pursue rehabilitation at Royalton Manor, and hospital staff began to prepare Ms. Garlanger for discharge to that facility. Pet'r's Ex. 7 at 1. On January 9, 2012, as part of the discharge process, Ms. Garlanger underwent a chest CT, which revealed a "2.9 cm right

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[10] An ANA, or antinuclear, antibody is an "antibod[y] directed against nuclear antigens; ones against a variety of different antigens are almost invariably found in systemic lupus erythematosus and are frequently found in rheumatoid arthritis, scleroderma . . ., Sjögren syndrome, and mixed connective tissue disease." *Dorland's* at 101.

[11] An SSA, or anti-SS-A, antibody is "an antinuclear antibody that occurs in Sjögren syndrome and systemic lupus erythematosus." *Dorland's* at 101.

[12] A lumbar puncture is "the withdrawal of fluid from the subarachnoid space in the lumbar region, usually between the third and fourth lumbar vertebrae, for diagnostic or therapeutic purposes." *Dorland's* at 1556.

[13] Cerebrospinal fluid is "[t]he fluid that flows in and around the hollow spaces of the brain and spinal cord, and between two of the meninges (the thin layers of tissue that cover and protect the brain and spinal cord)." CEREBROSPINAL FLUID, National Dictionary of Cancer Terms, National Cancer Institute (last visited Feb. 10, 2020), https://www.cancer.gov/publications/dictionaries/cancer-terms/def/cerebrospinal-fluid.

[14] An electromyography study is "an electrodiagnostic technique for recording the extracellular activity . . . of skeletal muscles at rest, during voluntary contractions, and during electrical stimulation . . .." *Dorland's* at 602.

lung lesion." *Id.* Ms. Garlanger had a consultation with Dr. Robert Piasecki, a pulmonologist, on January 12, 2012. *Id.* at 9. Dr. Piasecki noted that Ms. Garlanger had been "a pack a day smoker for 50 years[,]" but that she had "recently decreased that to a half pack per day." *Id.* An examination found Ms. Garlanger's upper extremity movements "erratic," and she reported an "[i]nability to sense anything in her hands and upper extremities or lower extremities." *Id.* Dr. Piasecki's impression was "[r]ight middle lobe nodule with significant hilar or mediastinal adenopathy . . ., possible small cell with paraneoplastic syndromes[15] (SIADH)[16] and sensory motor neuropathy." *Id.* Dr. Piasecki recommended a fiberoptic bronchoscopy[17] and referred Ms. Garlanger for an oncology consultation. *Id.*

On January 13, 2012, Ms. Garlanger was assessed by Dr. Susan DilanSzanto. Pet'r's Ex. 11 at 505. Dr. DilanSzanto noted Ms. Garlanger's long history of smoking, and Dr. DilanSzanto's impressions included "[g]eneralized inflammatory demyelinating polyneuropathy" and "SIADH." *Id.* at 506. Dr. DilanSzanto also wrote that, "[w]ith the inflammatory demyelination, lung nodule, [and] SIADH, consideration from GBS would now shift to the etiology of paraneoplastic syndrome[,]"which she felt was "most possibly small cell [carcinoma]." *Id.* On the same day, Ms. Garlanger underwent a bronchoscopy with Dr. Piasecki. Pet'r's Ex. 2 at 113. The results showed that the nodule was "suspicious" for small cell carcinoma. *Id.* at 107.

On January 14, 2012, Ms. Garlanger had another assessment with Dr. Ward. Pet'r's Ex. 2 at 58. Dr. Ward's impressions from this visit included "[p]redominantly demyelinating polyneuropathy with superimposed sensory neuronopathy[18]" that he felt was "highly suspicious for paraneoplastic syndrome." *Id.* at 59. Dr. Ward recommended waiting for final biopsy results and discussed with Ms. Garlanger's family the benefits of seeking a second opinion. *Id.*

On January 16, 2012, Ms. Garlanger was admitted to inpatient rehabilitation services, where she remained until March 23, 2012. *See generally* Pet'r's Ex. 1. On January 31, 2012, Ms. Garlanger underwent a paraneoplastic autoantibody evaluation, which was positive for "anti-

[15] Paraneoplastic syndrome is "a symptom-complex arising in a cancer-bearing patient that cannot be explained by local or distant spread of the tumor." *Dorland's* at 1843.

[16] SIADH is an acronym for "syndrome of inappropriate antidiuretic hormone secretion." Neil M. Davis, MEDICAL ABBREVIATIONS: 26,000 CONVENIENCES A T THE EXPENSE OF COMMUNICATION AND SAFETY 329 (12th ed. 2005). Antidiuretic hormone, or vasopressin, is "one of two nonapeptide hormones . . . [that] has a specific effect on the epithelial cells of renal collecting tubules, augmenting reabsorption of water independently of solutes to cause concentration of urine and dilution of blood serum." *Dorland's* at 870, 2027.

[17] A bronchoscopy is an "examination of the bronchi through a bronchoscope." *Dorland's* at 253. Bronchi is the "genitive and plural of *bronchus*[,]" *id.* at 251, which refers to "any of the larger air passages of the lungs . . .[,]" *id.* at 254.

[18] Neuronopathy is a "polyneuropathy involving destruction of the cell bodies of the neurons." *Dorland's* at 1268. Sensory neuronopathy is "degeneration of peripheral sensory neurons in the dorsal root ganglia, with inflammation and infiltration by lymphocytes, characterized by pain and numbness that begins in the limbs and may advance to the trunk and face. It may be a complication . . . of certain cancers, especially small cell lung carcinoma." *Id.*

neuronal nuclear antibody, type 1."[19] Pet'r's Ex. 11 at 488. The results noted that "this [finding] supports a paraneoplastic autoimmune neurological disorder." *Id.* Ms. Garlanger also received her lung biopsy results on this date from Dr. Thomas Sebo at the Mayo Clinic. *See* Pet'r's Ex. 5 at 56. Dr. Sebo wrote that Ms. Garlanger's "clinical features [were] strongly suggestive of small cell carcinoma of the lung." *Id.* However, he continued that, "[w]ithout that clinical bias, [he] would be hard pressed to classify the [biopsy results] as positive for small cell carcinoma[,]" although he did find "occasional clusters of cells present with cytologic features qualitatively diagnostic for small cell carcinoma." *Id.* He recommended that, if Ms. Garlanger's "physicians . . . [were] comfortable treating [her] as having small cell carcinoma, then [he thought the biopsy results] support[ed] that approach. Otherwise, further evaluation may be warranted." *Id.*

On February 3, 2012, Ms. Garlanger presented to Dr. Kourosh Rezania, a neurologist at the University of Chicago Medicine. Pet'r's Ex. 10 at 10. Dr. Renzania noted that Ms. Garlanger "looked chronically ill" upon presentation, and that "[t]here was evidence of diffuse muscle wasting." *Id.* at 11. An examination revealed decreased strength and minimal reflexes, with "no pathological reflexes . . . present[]" in her lower extremities. *Id.* A sensory examination revealed "severely impaired proprioception at the toes, ankles, and . . . fingers[,]" while "[v]ibratory sensation was absent at the knees . . .." *Id.* Ms. Garlanger also had "significantly impaired" pinprick sensation in her "bilateral upper and lower extremities up to proximal thighs and forearms." *Id.* Ms. Garlanger was in a wheelchair during this visit and was experiencing profound weakness such that her "stance and gait could not be evaluated . . .." *Id.* Dr. Rezania's impression was that, "[a]lthough [Ms. Garlanger's] clinical course [was] suggestive for a post[-]vaccination [GBS], the presence of the lung nodule and SIADH raises the possibility of a perineoplastic [(sic)] disease." *Id.* at 12. He planned on conducting a "repeat EMG and nerve conduction study to assess whether the neuropathy [was] axonal versus demyelinating." *Id.* The EMG results were "abnormal[,] demonstrating a sensory [over] motor polyneuropathy (predominantly axonal). . . . Given the clinical scenario, differential diagnosis include[d] GBS variant, other inflammatory or paraneoplastic neuropathies[, and/or] dorsal root ganglionopathy." *Id.* at 16.

On February 14, 2012, Ms. Garlanger had a follow-up with Dr. Ward. Pet'r's Ex. 5 at 46. Dr. Ward reviewed her medical history to date and Dr. Rezania's note. *Id.* Dr. Ward's impressions included "[p]redominantly sensory neuronopathy consistent with paraneoplastic process[,]" and "[q]uestionable post[-]vaccination [GBS] treated with Iv IgG [in] December[] 2011." *Id.* at 47. Dr. Ward referred Ms. Garlanger to palliative care and "discussed the merits of chemotherapy and radiation therapy." *Id.* Ms. Garlanger "seem[ed] interested in [obtaining] an opinion with regard to whether this would be helpful to her." *Id.*

Ms. Garlanger presented to Dr. Jason Beckrow, an oncologist, on March 16, 2012. Pet'r's Ex. 4 at 6. Upon presentation, Ms. Garlanger was "weak" and "in a wheelchair with poor motor function of the upper and lower extremities and reduced fine motor function . . .." *Id.* Dr. Beckrow's assessment was "recently-diagnosed small-cell lung cancer, localized stage at the time of initial workup." *Id.* at 8. He also noted a "[h]istory of [GBS], likely secondary to paraneoplastic

[19] Anti-neuronal nuclear antibody, type 1 is an "anti-Hu antibody," which is "any of the polyclonal IgG autoantibodies directed against the proteins of the Hu antigen family; they are associated with paraneoplastic sensory neuropathy and encephalomyelitis in small cell lung carcinoma . . .." *Dorland's* at 101.

syndrome secondary to" this diagnosis, as well as "SIADH, also likely secondary to" this diagnosis. *Id.* Dr. Beckrow recommended "that [Ms. Garlanger] receive chemotherapy at least on a trial basis," as "she would [potentially] find significant benefits, both in her motor function and electrolyte imbalances." *Id.* He also recommended palliative care and that Ms. Garlanger "be reviewed at an interdisciplinary tumor board." *Id.* at 8–9.

On April 20, 2012, Ms. Garlanger had a follow-up with Dr. Mancini. Pet'r's Ex. 5 at 25. Dr. Mancini noted that Ms. Garlanger had declined chemotherapy, instead "opting for a more natural approach," including Orasal. *Id.* Dr. Mancini's assessment included "metastatic small cell carcinoma of lung, with secondary demyelinating polyneuropathy/[GBS] and SIADH." *Id.* at 27.

Ms. Garlanger presented for a follow-up with Dr. Beckrow on May 4, 2012. Pet'r's Ex. 4 at 4. Dr. Beckrow wrote that Ms. Garlanger was doing "fairly well" on the Orasal, an "herbal remedy" that Dr. Beckrow was "not intimately aware of . . .." *Id.* An examination revealed improved strength, appetite, and "general wellbeing and performance status." *Id.* Dr. Beckrow directed Ms. Garlanger to continue the Orasal treatments and follow-up again in four weeks. *Id.* at 5.

On May 18, 2012, Ms. Garlanger had a follow-up visit with Dr. Mancini. Pet'r's Ex. 5 at 23. Dr. Mancini noted "increased strength" and that Ms. Garlanger was "doing better at eating solid foods[,]" although her "appetite [was] still not back . . .." *Id.* Dr. Mancini directed Ms. Garlanger to continue the Orasal treatments. *Id.* at 24. Ms. Garlanger had another follow-up visit with Dr. Mancini on June 15, 2012, during which Dr. Mancini wrote that Ms. Garlanger's "[s]trength [was] slowly improving" and that she was "drinking much more water." *Id.* at 21. Dr. Mancini directed Ms. Garlanger to continue the Orasal treatments and follow-up with oncology. *Id.*

On June 29, 2012, Ms. Garlanger presented for a follow-up with Dr. Beckrow. Pet'r's Ex. 4 at 2. Dr. Beckrow wrote that Ms. Garlanger "[was] doing exceptionally well" and was "[c]linically . . . relatively stable." *Id.* She "ha[d] a complaint of a cough, with minimal sputum production . . . largely because of her poor respiratory effort." *Id.* Dr. Beckrow planned to have Ms. Garlanger continue her herbal treatment and follow-up in one month. *Id.* at 3.

Ms. Garlanger had an additional follow-up with Dr. Mancini on July 13, 2012. Pet'r's Ex. 5 at 18. Ms. Garlanger reported feeling "very sleepy," and Dr. Mancini noted that she was "getting weaker." *Id.* Dr. Mancini's examination found weakness in all of Ms. Garlanger's extremities and "audible gurgling with respirations." *Id.* at 19. Dr. Mancini recommended palliative care, but Ms. Garlanger's family declined that option. *Id.*

On July 30, 2012, Ms. Garlanger presented to the emergency room because of shortness of breath. Pet'r's Ex. 11 at 89. Her condition continued to deteriorate, and she was transferred to hospice care on August 4, 2012. Ms. Garlanger passed away on August 5, 2012. Pet'r's Ex. 9 at 1. Her death certificate lists "[a]cute [p]neumonia" and "[n]euroendocrine [l]ung [c]ancer" as conditions that directly caused her death. *Id.* at 2. The death certificate also lists "[p]araneoplastic [s]yndrome with [GBS]" and "[c]ongestive [h]eart [f]ailure" as significant conditions that contributed to her death but did not result in the underlying cause of her death. *Id.*

III. Expert Review

A. Petitioner's Expert, Lawrence Steinman, M.D.

Dr. Steinman received his medical degree from Harvard in 1974. Pet'r's Ex. 13 at 1. He completed his post-graduate training at Stanford University, where he completed an internship in surgery in 1973, a residency in pediatrics in 1974, and a residency in pediatric and adult neurology from 1977 to 1980. *Id.* He became board-certified in neurology in 1984. *Id.* at 14. He currently serves as a professor of pediatrics and genetics in Stanford's Department of Neurology and Neurological Sciences. *Id.* He explained that his clinical practice involves "see[ing] patients on [(sic.)] both adult and pediatric neurology." Tr. 11:4–5. Dr. Steinman stated that he has "published extensively in peer-reviewed journals[,]" Tr. 11:18–19, and his curriculum vitae includes over four-hundred and fifty published articles of which he is a listed author, Pet'r's Ex. 13 at 4–40. He also explained that he has "testified many times in [the Office of Special Masters]." Tr. 12:12.

Dr. Steinman submitted four expert reports and testified during the entitlement hearing. *See* Pet'r's Exs. 12, 28, 32, 36; Tr. 10:12–56:10. I recognized Dr. Steinman as an expert in neurology and immunology with no objection from Respondent. Tr. 14:5–9.

In his first report, Dr. Steinman wrote that "[i]t [was his] opinion, to a high degree of medical certainty[,] that the [flu] vaccine [Ms. Garlanger received] on Oct[ober] 15, 2011[,] triggered [her] GBS." Pet'r's Ex. 12 at 15. He argued that "[a]n antibody response to myelin basic protein, triggered by molecular mimicry between [the flu vaccine] and myelin basic protein, [was] the best scientific insight that provides a mechanistic basis into how [Ms.] Garlanger developed GBS." *Id.*

During his testimony, Dr. Steinman stated that "molecular mimicry is established for [GBS]." Tr. 22:17. He wrote that "[t]he most well-known example of molecular mimicry as a causative mechanism for autoimmune disease occurs after injection with campylobacter jejuni." Pet'r's Ex. 12 at 8. He explained that campylobacter jejuni is "an infection that causes diarrhea[and] gastrointestinal distress . . . that shares sugars that are on the coating of your nerves, and that's an example of molecular mimicry caused by infection." Tr. 22:14–16.

Dr. Steinman provided two articles to support vaccine-induced GBS. The first is by Schonberger et al., which provides an in-depth review of GBS cases following the A/New Jersey flu vaccination program in 1976–77. Pet'r's Ex. 26[20] at 1. The authors "uncovered a total of 1098 patients with onset of GBS from October 1, 1976, and January 31, 1977, from all [fifty] states, [the] District of Columbia, and Puerto Rico." *Id.* Of those cases, "[a] total of [five-hundred and thirty-two] patients had recently received an A/New Jersey [flu] vaccination prior to their onset of GBS . . .." *Id.* After reviewing epidemiological data of the total GBS cases cited in the paper, the authors found that, "when compared to the unvaccinated population, the vaccinated population

[20] Lawrence B. Schonberger et al., *Guillain-Barre Syndrome Following Vaccination in the National Influenza Immunization Program, United States, 1976–1977*, 110(2) AM. J. OF EPIDEMIOLOGY 105 (1979).

had a significantly elevated attack rate in every adult age group." *Id.* Therefore, they concluded "that many cases of GBS were related to vaccination." *Id.*

The second paper is by Langmuir et al. Pet'r's Ex. 27.[21] The authors conducted a similar review of GBS cases following the A/New Jersey/76 flu vaccine campaign. *Id.* at 1. The authors reviewed data "summaries of approximately 1,300 cases reported as [GBS] by state health departments . . . following the swine [flu] vaccination program in 1976–1977 . . .." *Id.* Based on this review, the authors created a system of "classification according to [the] extent of motor involvement" seen in each patient. *Id.* They found that "cases with 'extensive' paresis or paralysis occurred in a characteristic epidemiologic pattern closely approximated by a lognormal curve, suggesting a causal relationship between the disease and the vaccine." *Id.* They continued that "[c]ases with 'limited' motor involvement showed no such pattern, suggesting that this group included a substantial proportion of cases which were unrelated to the vaccine." *Id.*

Dr. Steinman testified that "[t]he logical progression [of Ms. Garlanger's vaccine-induced GBS] is she got the [flu] shot, an immune response developed, it's cross-reactive and, therefore, inflammatory neuropathy starts up." Tr. 25:1–5. He explained that "[t]he immunity attacks [Ms. Garlanger's] nerves, specifically the peripheral nerve, giving her[] . . . both motor and sensory findings." Tr. 24:2–4. Dr. Steinman stated that the CSF testing, which showed the presence of myelin basic protein, demonstrates "that myelin was being injured, thereby releasing that protein, which normally you don't find in the spinal fluid of a healthy individual . . .." Tr. 35:14–17. Dr. Steinman opined that this finding "fits with Petitioner's theory." Tr. 35:19–20.

Dr. Steinman wrote that Ms. Garlanger developed GBS in a time frame "consistent with epidemiological studies . . . undertaken during the Swine Flu epidemic." Pet'r's Ex. 12 at 15. The paper by Schonberger et al. found that "[t]he period of increased risk [of developing vaccine-induced GBS] was concentrated primarily within the [five]-week period after vaccination, although it lasted for approximately [nine] or [ten] weeks." Pet'r's Ex. 26[22] at 1. The Langmuir et al. paper found that "[t]he effect attributed to the [flu] vaccine lasted for at least six weeks and possibly for eight weeks, but not longer." Pet'r's Ex. 27[23] at 1. Dr. Steinman argued that Ms. Garlanger's onset "fits within either" of these time frames. Tr. 26:7–8.

Dr. Steinman acknowledged that "there is sufficient evidence to conclude that [Ms.] Garlanger suffered from a paraneoplastic syndrome secondary to a presumed small cell lung carcinoma." Pet'r's Ex. 12 at 8. He continued, "[t]he inappropriate [antidiuretic hormone] ADH is a concomitant of small cell lung carcinoma." *Id.* He noted "the likelihood of [a] small cell carcinoma [diagnosis was] reasonable[]" based off of Ms. Garlanger's positive anti-Hu antibody test. *Id.* However, Dr. Steinman also wrote in the same report that Ms. Garlanger's treating physicians only suggested this diagnosis, but it was never "confirmed by the pathologists." *Id.* He reproduced the Mayo Clinic pathologist's report in full, which concluded that Ms. Garlanger's "clinical features are strongly suggestive of small cell carcinoma of the lung." *Id.* at 7 (quoting

[21] Alexander D. Langmuir et al., *An Epidemiologic and Clinical Evaluation of Guillain-Barré Syndrome Reported in Association with the Administration of Swine Influenza Vaccines*, 119(6) AM. J. OF EPIDEMIOLOGY 841 (1984).
[22] Schonberger et al., *supra* note 20.
[23] Langmuir et al., *supra* note 21.

Pet'r's Ex. 5 at 56). The pathologist continued that, "[w]ithout that clinical bias, [he] would be hard pressed to classify [the diagnostic findings] as positive for small cell carcinoma." *Id.* Dr. Steinman wrote that, "[s]ince the diagnosis of small cell carcinoma was inferential, and the vaccine was a definitive fact," he therefore "[gave] the highest importance for the cause of GBS to the [flu] vaccine . . .." *Id.* at 16. He also wrote that Ms. Garlanger's "paraneoplastic syndrome, with the presence of anti-Hu antibodies, may have worsened [her] course, already in process with two weeks after her [flu] vaccine." *Id.*

Dr. Steinman did not explain what a paraneoplastic syndrome is in his reports or his testimony, aside from stating that they are "related . . . to cancer." Tr. 28:3–4. However, he submitted articles with his first report that provide further explanation of this syndrome. The first is by Bhat and Steinman. Pet'r's Ex. 17. [24] The article is a "review focus[ing] on the autoimmune diseases where the brain and spinal cord are attacked." *Id.* at 1. The authors explain that paraneoplastic syndromes result when "adaptive immune responses target cancer antigens that are shared with structures in the nervous system, resulting in some characteristic neurological conditions . . .." *Id.* They wrote that "[t]he most common example of a paraneoplastic syndrome is the cerebellar syndrome, where clinical findings include ataxia and tremor . . . in some individuals with ovarian cancer." *Id.* at 8. The authors also note that some "[o]ther forms of paraneoplastic cerebellar disease have anti-Hu antibodies." *Id.* They wrote that "[o]ften the neurological disorder becomes apparent before there is any diagnosis of malignancy." *Id.*

The second article is authored by Dr. Steinman and is titled *Conflicting Consequences of Immunity to Cancer versus Autoimmunity to Neurons: Insights from Paraneoplastic Disease*. Pet'r's Ex. 18.[25] In it, Dr. Steinman provides a review of an article, not in evidence, that appeared in the same issue of the European Journal of Immunology in 2014. *Id.* at 2. Dr. Steinman wrote that "[m]ost . . . paraneoplastic diseases involve neuronal autoimmunity due to a tumor antigen, often intracellular, that is shared with the nervous system." *Id.* He noted that paraneoplastic syndromes are "often [associated with] small cell lung carcinoma or a gynecological tumor." *Id.* at 1–2.

Dr. Steinman also wrote in his first expert report that anti-Hu antibodies "are associated with GBS." Pet'r's Ex. 12 at 15. To support this assertion, he provided a paper by Camdessanche et al., in which the authors "conducted a retrospective study of [twenty] patients[]" for the purposes of "investigat[ing] the clinical and electrophysiological manifestations of neuropathies associated with anti-Hu antibodies . . .." Pet'r's Ex. 25 at 1.[26] The authors found that, out of these twenty patients, "[c]ancer was found in [seventeen][,]" with thirteen of these patients having small cell lung cancer. *Id.* at 4. They also found that "[p]eripheral neuropathy was the presenting symptom of the paraneoplastic neurological syndrome in [nineteen] . . . cases, and the only manifestation in six [cases] . . .." *Id.* at 4. They wrote that "[t]he neuropathy was clinically purely sensory in [fourteen] patients . . ., sensorimotor in five [patients] . . ., and purely motor in one [patient] . . .."

[24] Roopa Bhat & Lawrence Steinman, *Innate and Adaptive Autoimmunity Directed to the Central Nervous System*, 64 NEURON 123 (2009).
[25] Lawrence Steinman, *Immunity to Cancer versus Autoimmunity to Neurons: Insights from Paraneoplastic Disease*, 44 EUR. J. IMMUNOL. 3201 (2014).
[26] Jean-Philippe Camdessanche et al., *Paraneoplastic Peripheral Neuropathy Associated with Anti-Hu Antbodies: A Clincal and Electrophysiological Study of 20 Patients*, 125 BRAIN 166 (2002).

Id. The authors discussed one patient who "had an acute ascending sensorimotor neuropathy resulting in complete paraplegia and severe proximal upper limb motor deficit associated with dysautonomic involvement." *Id.* They noted that this patient's "disorder resembled [GBS] but showed no improvement with follow-up." *Id.* The authors wrote that this patient "had slowing of the [motor conduction velocities ("MCVs")] that fell in the range for primary demyelination." *Id.* However, they concluded that this patient's "clinical and electrophysiological data suggested a pure peripheral neuropathy and not encephalomyelitis . . .." *Id.* Regarding electrophysiological data for anti-Hu associated neuropathies, the authors wrote that most patients' "sensory nerves were abnormal[,]" as were their "motor nerves." *Id.* The authors argued that these findings "suggest that . . . the pathological process is frequently not restricted to dorsal root ganglia and is probably more complex." *Id.* at 4–5. The authors concluded that "the typical pattern of sensory neuronopathy is rare and that the presence of axonal/demyelinating pattern does not exclude the diagnosis of paraneoplastic anti-Hu neuronopathy." *Id.* at 5. Aside from the discussion of the single patient with GBS-like presentation, the authors did not discuss any association between anti-Hu antibodies and GBS.

During his testimony, Dr. Steinman noted that Ms. Garlanger's anti-Hu antibody testing was conducted subsequent to the IVIg treatment, which he stated "can disturb, distort, [or] induce spurious antibody results." Tr. 34:7–11. However, he stated on cross examination that he thought Ms. Garlanger's anti-Hu antibody test result was "a true positive." Tr. 41:6–8.

Dr. Steinman also testified that "SIADH . . . is one of the hallmarks of small cell lung carcinoma. It secretes endocrine factors like antidiuretic hormone." Tr. 28:19–21. Dr. Steinman stated that this condition "is associated with [GBS] just as much – I wouldn't say just as much, but just as well." Tr. 28:25–29:2. Dr. Steinman explained that SIADH is also "associated" with valproic acid, which Ms. Garlanger was taking. Tr. 29:23–25. Dr. Steinman was unable to assert causation in this context, noting that he "[doesn't] know if the drug does it or [the] associated disorder does . . .." Tr. 30:2–3. Dr. Steinman did not, however, file any medical literature to support these assertions.

In his first supplemental expert report, Dr. Steinman wrote "[i]t may help the court in this matter to consider one other alternative. If not for the [flu] vaccine . . . , [Ms. Garlanger] would not have suffered her paraneoplastic related neuropathy." Pet'r's Ex. 28 at 7. He continued, "[i]n this sense, the [flu] immunization would have been the 'aggravating factor' that ended decades of dormancy of her disease, only to become manifest weeks after the immunization." *Id.* at 7–8. He explained during my questioning that Ms. Garlanger "had the cancer for a long time and then it wasn't that the cancer was aggravated, but that a manifestation of the cancer was aggravated by getting the flu shot." Tr. 54:15–18. I then asked him if "the manifestation would be paraneoplastic syndrome or GBS[,]" to which he responded "GBS." Tr. 54:19–21. He also stated that "it's more compatible, the set of facts, to talk about this [case] in terms of significant aggravation. And then . . . the aggravation was the emergence of the syndrome that's associated with cancer . . .." Tr. 55:23–56:2.

In his first export report, Dr. Steinman wrote that Ms. Garlanger had "presumed small cell carcinoma[,]" but also called it a "tentative diagnosis" and reproduced the pathology report in its entirety to conclude that "the diagnosis of small cell carcinoma was inferential . . .." Pet'r's Ex.

12 at 8, 16. During his testimony, Dr. Steinman read the pathology report into the record and concluded "that the diagnosis was less than [one hundred] percent." Tr. 19:22–21:12. However, he also stated on cross examination that the cancer type "doesn't matter that much" to him. Tr. 40:4–8. I asked Dr. Steinman whether his focus on the cancer type was "a preemptive response to [Respondent's arguments] or [whether] it matter[ed] what kind of cancer [Ms. Garlanger] had?" Tr. 55:14–15. Dr. Steinman responded that Ms. Garlanger "could have had the paraneoplastic syndrome if it was lung cancer, non-small cell[,] . . . [s]o I guess that would fall into the realm, it doesn't matter." Tr. 55:16–19.

B. Petitioner's Expert, Gregory Arov, D.O.

Dr. Arov received his medical degree from the Lake Erie College of Osteopathic Medicine in 2006. Pet'r's Ex. 34 at 1. He completed an internship at Advocate Lutheran General Hospital in Park Ridge, Illinois, in 2007, a residency at John Peter Smith Hospital in Fort Worth, Texas, in 2011, and a fellowship at the University of Wisconsin-Madison in 2012. *Id.* Dr. Arov is board certified in radiology by the American Osteopathic Board of Radiology. *Id.* He is currently a clinician at Universal Radiology Services, LLC. *Id.*

Dr. Arov submitted one expert report in this case but did not testify at the entitlement hearing. *See* Pet'r's Ex. 33.

Dr. Arov reviewed Ms. Garlanger's chest x-rays dated November 28, 2011 and January 9, 2012. *Id.* In Dr. Arov's opinion, the x-ray conducted on November 28, 2011, showed "a 14.5 mm density seen within the right lower lobe." *Id.* The x-ray conducted on January 9, 2012, showed that "[a] faint, poorly defined density is seen within the right lower lobe[,] which appears to have increased in size when compared to the prior exam." *Id.* Dr. Arov also reviewed a CT of Ms. Garlanger's chest conducted on January 10, 2012. *Id.* Dr. Arov wrote that this test showed "a 29 mm mass within the anterior aspect of the right middle lobe." *Id.* Lastly, Dr. Arov reviewed a CT of Ms. Garlanger's head and wrote that there was no evidence of "acute intracranial process." *Id.*

Dr. Arov did not submit any additional information on these findings. *See id.*

C. Respondent's Expert, Sara Vargas, M.D.

Dr. Vargas graduated from the University of Vermont College of Medicine in 1994. Resp't's Ex. B at 1. She completed a residency in anatomic and clinical pathology at Brigham and Women's Hospital, and a fellowship in pediatric pathology at Children's Hospital in Boston, Massachusetts. *Id.* She is board-certified in anatomic and clinical pathology and in pediatric pathology. Tr. 166:7–8. She currently serves as an associate professor at Harvard Medical School. Resp't's Ex. B at 1. Her clinical responsibilities include "sign[ing] pathology reports, evaluat[ing] pathology cases and sign[ing] the reports only for lung cases[,]" as well as serving as a "general pediatric pathologist . . . with a special emphasis on [the] lung." Tr. 166:14–19. Dr. Vargas stated that she is involved with diagnosing patients with lung cancer, and specifically small cell lung carcinoma. Tr. 166:20–25. She also stated that she conducts research and publishes articles on lung cancer. Tr. 167:1–6.

Dr. Vargas submitted two expert reports and testified at the entitlement hearing. *See* Rep't's Exs. A, F; Tr. 165:13–184:7. I recognized Dr. Vargas as an expert in anatomic pathology and lung pathology without objection from Petitioner. Tr. 167:7–15.

In her first expert report, Dr. Vargas wrote that "[t]here is convincing and virtually irrefutable evidence that [Ms. Garlanger] had carcinoma of the lung . . .." Resp't's Ex. A at 6. Dr. Vargas explained that "[c]arcinoma of the lung is the most diagnosed noncutaneous cancer," and is divided into two subgroups, small cell and non-small cell. *Id.* She wrote that "[s]mall cell carcinoma is known in particular for a tendency to present at a stage already spread beyond the lung . . ., even when the primary pulmonary nodule is still quite small." *Id.* Dr. Vargas submitted a book chapter with her first report which explained that "[t]he overwhelming clinical, epidemiologic, and experimental evidence implicates cigarette smoking in the etiology of lung cancer[,]" and that "the association [between smoking and lung cancer] is strongest for squamous cell carcinomas and small-cell carcinomas . . .." Resp't's Ex. A, Tab 6, at 2.[27]

Dr. Vegas explained that "[c]ytopathology . . . is a branch of pathology that involves the study of cells. . . ., focus[ing] on the study of samples with small amounts of cellular material[], such as those recovered from . . . a fine needle aspirate." *Id.* Dr. Vargas wrote that "[d]iagnoses in cytopathology are typically less concerned with identifying cancer subtypes," instead focusing "on whether or not cancer cells are found." *Id.* She explained that, "[i]n the first line of a cytopathology report, a pathologist typically indicates one of the following categories (in [the] same or similar language): 1. Positive for malignancy[;] 2. Suspicious for malignancy[;] 3. Negative for malignancy[;] 4. Insufficient for evaluation." *Id.* at 6–7. The "positive for malignancy" category, Dr. Vargas continued, "is the highest level of certainty for malignancy available in the field." *Id.* at 7. Dr. Vargas noted that both she and Dr. Sebo selected this category after analyzing Ms. Garlanger's cell samples. *Id.*

Dr. Vargas opined that there is "compelling evidence that [Ms. Garlanger's carcinoma] was of the small cell type." *Id.* at 6. She wrote that "[s]ubtyping lung cancer via cytopathology is challenging. . . . [because] there are combined types of lung carcinoma." *Id.* at 7. She explained that, "[b]ecause of such tumor heterogeneity, a small sample . . . may show carcinoma cells without the appearance of small cell subtype, even in cases of bona fide small cell carcinoma." *Id.* Dr. Vargas opined that, "[f]rom this perspective, the specific subtype of malignant cells identified in [Ms.] Garlanger's [sample] is not critical in determining which type lung carcinoma was present." *Id.* She explained that the "positive for malignancy" category selection, taken with "with the clinical presentation of a small lung tumor, already spread to [the] lymph nodes, associated with SIADH as well as neurologic symptoms and anti-Hu antibodies," makes small cell carcinoma "the most likely subtype of [Ms. Garlanger's] lung carcinoma." *Id.* Dr. Vargas argued that "[i]f [Ms. Garlanger's] clinicians had not been satisfied with the clinicopathologic diagnosis of small cell carcinoma, a re-biopsy would have been required before cancer treatment could be offered." *Id.* However, Dr. Vargas noted that "Mrs. Garlanger's clinical team[felt that] the likelihood that the carcinoma subtype was small cell was high enough that another biopsy was not sought." *Id.*

[27] Charalambos C. Solomides et al., *Respiratory Tract*, *in Comprehensive Cytopathology* 247 (M. Bibbo & D. Wilbur eds., 4th ed.).

Dr. Vargas explained that paraneoplastic syndromes are "brain, spinal cord, and nerve-based problems associated with cancer." *Id.* She noted that "[t]hey are most commonly associated with lung carcinoma[] and may occur in up to [thirty percent] of lung carcinoma patients, most commonly in the setting of small cell carcinoma . . .." *Id.* Dr. Vargas submitted a book chapter by Stefens-Swana et al., in which the authors conducted a "study on paraneoplastic neurological syndromes [("PNS")] in lung cancer[]" to "evaluate the frequency, clinical PNS manifestation, and association with well-characterized onconeural antibodies and other autoimmune reactions in such patients." Resp't's Ex. A, Tab 7, at 2.[28] The authors noted that "[l]ung cancer is recognized as one of the most frequent malignancy associated with classical and non-classical [PNS]." *Id.* They explained that "[l]imbic encephalitis, paraneoplastic cerebellar degeneration, Lambert-Eaton myasthenic syndrome, subacute sensory neuropathy, opsoclonus/myoclonus syndrome, and dermatomyositis are recognized as classical PNS, because their presence strongly suggests association with malignancy." *Id.* They also noted that "[d]etection of anti-Hu [and other onconeural antibodies] . . . enables a definite PNS diagnosis, even if the underlying malignancy is not identified." *Id.* The authors reviewed "[f]ifty consecutive lung cancer patients . . . with the PNS diagnosis . . .." *Id.* at 3. They performed "[t]esting for the presence of onconeural antibodies[,]" as well as "[n]euroimaging, neurophysiological, [CSF examination, and other laboratory tests" on these patients. *Id.* They found that "[sixty-four percent] of the lung cancer patients [had] signs of neurological deficits." *Id.* They also found that "[c]lassical [PNS] . . . in [thirty percent] of patients[,]" while patients with non-classical PNS had it manifest as "motor neuron disease . . ., upper motor neuron syndrome . . ., neuropathy . . ., [and] sensomotoric neuropathy . . .," among others. *Id.* They also found an autoimmune reaction in forty-two percent of the patients studied, with "anti-Hu antibod[ies] . . . found in [sixteen percent] of subjects . . .." *Id.* They also discussed that, in the fourteen small-cell lung cancer patients, "[fifty percent] manifested symptoms of both classical and non-classical PNS associated only with the presence of the well-characterized onconeural antibodies." *Id.* at 4. The authors concluded that "PNS signs in lung cancer patients have both classical and non-classical features." *Id.* at 1. They also concluded that "[t]he presence of well-characterized onconeural antibodies is strongly associated with classical features of PNS." *Id.*

Although Dr. Vargas wrote that "[t]he precise mechanism by which" paraneoplastic syndromes arise is "not completely known," she nonetheless described a process of "molecular mimicry," whereby "the immune response mounted by the body against cancer cells attacks nervous system cells as well as the cancer." *Id.* Dr. Vargas continued that "[s]mall cell carcinoma has 'neuroendocrine' features, a likely cancer subtype to share antigens with cells of the neurologic system . . .."

Dr. Vargas opined that Ms. Garlanger's paraneoplastic syndrome was evidenced by her "sensory and motor neuropathy, ataxia, autonomic dysfunction, possible lower motor neuron disease, and syndrome of inappropriate secretion of anti-diuretic hormone." Rep't's Ex. A at 8. Dr. Vargas acknowledged that "[a] subset of these findings can be found in [GBS], and therefore [GBS] comes into the differential diagnosis of paraneoplastic neurologic syndromes." *Id.* However, Dr. Vargas noted that "some authors . . . view [GBS] or [GBS]-like syndrome in the

[28] P. Stefens-Swana et al., *Neurological Paraneoplastic Syndromes in Lung Cancer Patients, in Respiratory Regulation – The Molecular Approach* 333–39 (M. Pokorski ed.).

setting of carcinoma to represent a paraneoplastic syndrome." *Id.* (citing Respt's' Ex. A, Tab 5;[29] Resp't's Ex. A, Tab 1).[30] Dr. Vargas cited a book chapter by Koike and Sobue, in which the authors briefly discussed GBS in the presence of cancer. Resp't's Ex. A, Tab 5, at 5. They noted that "rare types of neuropathy, including GBS, . . . can also occur as paraneoplastic syndrome and manifest as sensory-motor neuropathy." *Id.* They wrote that "[m]ost cases of GBS are preceded by vaccination or by respiratory or gastrointestinal infections, but . . . may also occur in the setting of malignancies." *Id.* They continued, "[w]hether GBS arises as a result of the underlying cancer or whether this is simply a chance association is still under debate." *Id.* They noted that "GBS has been more commonly associated with lymphomas as well as various kinds of solid tumors, such as small[-]cell lung cancer . . .." *Id.* They also noted that, when discussing one study that is not currently in evidence, "[a]cute mortality was significantly higher in patients with GBS and cancer when compared with those with GBS alone." *Id.*

Dr. Vargas also discussed the presence of anti-Hu antibodies in Ms. Garlanger's serum and noted that they "are present in approximately half of patients with paraneoplastic neurologic syndrome and small cell lung cancer." *Id.* at 8. Dr. Vargas cited the Koike and Sobue book chapter to assert that, when a patient demonstrates symptoms associated with a sensory neuropathy, "anti-Hu antibodies are seen in nearly all patients." *Id.* (citing Resp't's Ex. A, Tab 5, at 7).[31] Koike and Sobue wrote in their chapter that "the estimated specificity and sensitivity of anti-Hu antibody for sensory neuropathy of paraneoplastic etiology is [ninety-nine percent] and [eighty-two percent], respectively." Resp't's Ex. A, Tab 5, at 7. Dr. Vargas also wrote that, in anti-Hu small cell carcinoma, "it is most common for the symptoms of paraneoplastic neurologic syndrome to precede detection of the malignancy." *Id.* (citing Resp't's Ex. A, Tab 3, at 4).[32]

Dr. Vargas concluded that "[t]here is no reason to implicate vaccination as a cause of [Ms. Garlanger's] many neurologic findings." *Id.*

D. Respondent's Expert, Dr. Eric Lancaster

Dr. Lancaster received his doctoral degree in neuroscience in 2002 and his medical degree in 2003, both from the University of Maryland. Resp't's Ex. D at 1. Dr. Lancaster completed a neurology residency and a neuromuscular fellowship at the University of Pennsylvania in 2007 and 2008, respectively. Resp't's Ex. C at 1. He is board certified in neurology and has completed the neuromuscular medicine subspecialty board and an additional subspecialty board "focused on the proper performance of electrodiagnostic studies." *Id.* Dr. Lancaster is "an author on [twenty-two] peer-reviewed publications[,]" with his more "recent publications mostly concern[ing] autoimmune neurological disorders, particularly autoimmune encephalitis, and their mechanisms." *Id.* Dr. Lancaster noted that he has "written extensively about . . . paraneoplastic disorders." *Id.* He explained that his "current research projects and clinical practice focus on autoimmune and

[29] Haruki Koike & Gen Sobue, *Paraneoplastic Neuropathy, in Handbook of Clinical Neurology* 713 (G. Said and C. Krup eds.).
[30] Josep Dalmau & Myrna R. Rosenfeld, *Overview of Paraneoplastic Syndromes of the Nervous System*, retrieved from www.uptodate.com.
[31] Koike & Sobue, *supra* note 29.
[32] Josep Dalmau & Myrna R. Rosenfeld, *Paraneoplastic Syndromes Affecting the Spinal Cord and Dorsal Rot Ganglia*, retrieved from www.uptodate.com.

paraneoplastic disorders, detection and characterization of paraneoplastic antibodies, . . . and similar projects." Tr. 57:16–21. Dr. Lancaster is "currently an Assistant Professor of Neurology at the University of Pennsylvania[,]" Resp't's Ex. C at 1, where he "lecture[s] frequently on autoimmune and paraneoplastic disorders, autoimmune encephalitis, and similar disorders[,]" Tr. 59:10–12.

Dr. Lancaster submitted three expert reports and testified at the entitlement hearing. *See* Resp't's Exs. C, E; Tr. 57:1–162:25. I admitted Dr. Lancaster as an expert in neurology, neuroimmunology, and electrodiagnostic medicine without objection from Petitioner. Tr. 59:13–22.

Dr. Lancaster described GBS as "an autoimmune neuropathy that presents with sudden weakness and numbness, often ascending from the feet over a period of days." Resp't's Ex. C at 11. He wrote that the GBS "[p]atients typically reach peak disability within [two]-[three] weeks, with [four] weeks considered a maximum time period for progression." *Id.* He continued that GBS "[p]atients typically slowly recover[] over a course of months[,]" but "some patients have delayed or incomplete recovery . . .." *Id.* Dr. Lancaster explained that GBS patients "show[] specific demyelinating factors on nerve conduction studies[,]" including "severe slowing of conduction along the nerves and conduction block (failure of conduction across a particular nerve segment)." *Id.* As the disease progressed, Dr. Lancaster stated that clinicians "would see on the needle EMG signs of denervation in the muscle, signs that [the muscles] lost those motor fibers." Tr. 86:10–12. Dr. Lancaster noted that this finding "would actually become clearer over time. [It] wouldn't necessarily be totally apparent on the first [EMG study], but would become apparent on subsequent [studies]." Tr. 86:15–16.

Alternatively, Dr. Lancaster wrote that paraneoplastic syndromes "occur in patients with cancer[]" and "do not appear to be due to direct invasion of the nervous system by the neoplasm (tumor) . . .." Resp't's Ex. C at 12. Dr. Lancaster explained that paraneoplastic syndromes are thought to be "autoimmune," and explained that a "discover[y] supporting this hypothesis [is] the discovery of autoantibodies, such as 'anti-Hu' in some patients with paraneoplastic disorders." *Id.* He testified that the Hu protein "is an intracellular protein that's expressed in many cells . . . that [cells] use to handle intracellular functions like processing RNA . . .." Tr. 61:6–9. He explained that anti-Hu antibodies "are a very important marker of the anti-Hu paraneoplastic syndrome. Particularly at a titer greater than [one] to 1,000, they are very strongly predictive of a paraneoplastic syndrome." Tr. 62:4–7. Dr. Lancaster wrote that the anti-Hu antibody "was first found in patients with sensory neuronopathy and small cell lung cancer[,]" and are "very strongly associated" with these conditions. Resp't's Ex. C at 12.

In his first report, Dr. Lancaster cited a paper by Dalmau et al., which found that "[seventy-seven-and-one-half percent] of patients with anti-Hu syndrome turn out to have small cell lung cancer." *Id.* (citing Resp't's Ex. C, Tab 6).[33] In that article, the authors "undertook to study the clinical course of . . . [seventy-one] patients with [paraneoplastic encephalomyelitis ("PEM")]/[paraneoplastic sensory neuronopathy ("PSN"], to determine the nature of the underlying tumor, the spectrum of neurologic symptoms, the response of neurologic symptoms to

[33] Josep Dalmau et al., *Anti-Hu–Associated Paraneoplastic Encephalomyelitis/Sensory Neuropathy: A Clinical Study of 71 Patients*, 71(2) MEDICINE 59 (1992).

treatment, the outcome of both the paraneoplastic disease and the tumor, and the principal cause of death." Resp't's Ex. C, Tab 6, at 1. Of these patients, the authors found that "[i]n [fifty-five] patients . . . the associated tumor was a[] [small-cell lung cancer,]" which "[a]t the time . . . [of] diagnos[is] . . . was limited to the chest in [fifty-three] patients . . ., with metastases outside the chest in [two] . . .." *Id.* at 4. The authors also found that "[s]ensory symptoms were the first complaint in [forty-two] patients[,]" while "[twenty-three patients] . . . had paresthesias in the hands and feet, [thirteen patients] . . . in the trunk, and [two . . . in the face." *Id.* at 5. The authors also noted that "[d]ysesthesias were described by [sixteen] patients . . ., and pain was associated in [nine] . . .." *Id.* They also wrote that "[b]ack and/or radicular pain, and flexor spasms, were described by some patients." *Id.* The authors described the course of the neurological symptoms as "a relentless progression" in "the majority" of patients, while "more rarely, intermittent progression of the symptoms, which eventually stabilized[]" occurred. *Id.* at 5–6. While discussing the predominant neurologic syndromes, the authors wrote that "[s]ensory neuropathy was present in [fifty-two patients. . .[,]" although "in only [forty-four patients] was PSN the predominant symptom." *Id.* at 6. They also wrote that "[m]otor neuron dysfunction was a predominant symptom[] in [fourteen] patients[,]" although they noted that [n]one developed a 'pure' motor neuron syndrome . . .." *Id.* The authors reviewed EMG results for twenty-three patients, of which twenty were abnormal. *Id.* at 7. In terms of patient outcomes, the authors wrote that "[t]he median time between first neurologic symptom and death was [seven] months . . .." *Id.* at 8. Based on their study, the authors concluded that:

> Patients with rapidly developing sensory neuropathy or symptoms of encephalomyelitis should be studied for the presence of the anti-Hu antibody; if the antibody is found, the possibility of small-cell lung cancer should be investigated. If a tumor is not found in the initial search, one may become evident in several months.

Id. at 13

Dr. Lancaster noted that the anti-Hu antibodies "are not thought to cause the syndrome themselves. They are a marker of the immune system being activated and the actual damage to the nervous system is likely due to other aspects of the immune system, such as killer T cells." Tr. 62:11–15. In support of this proposition, Dr. Lancaster cited to a paper by Sillevis Smitt et al., which found that "the antibodies do not make experimental animals sick when actively created by immunization or when human antibodies are passively transferred." Resp't's Ex. C at 12 (citing Resp't's Ex. C, Tab 2).[34] Once these T cells kill the neurons, Dr. Lancaster explained that "[t]here is no mechanism to recover these cells . . ., so the sensory deficits are severe and persistent." *Id.* at 13. This is why, according to Dr. Lancaster, "recovery is often limited in the sensory-predominant neuropathy syndrome of anti-Hu [syndrome] in comparison to GBS." *Id.*

Dr. Lancaster explained that "[t]he most common neurological syndrome associated with high titer anti-Hu is sensory-predominant neuronopathy[,]" i*d.* at 13, which he explained is "damage to the sensory neurons . . . [that] send[s] a process out to peripheral tissues to detect pain, temperature, touch, vibration and position[,]" Tr. 63:4–10. He continued, "when [the sensory

[34] P.A.E. Sillevis Smit et al., *Immunization with the Paraneoplastic Encephalomyelitis Antigen HuD Does Not Cause Neurologic Disease in Mice*, 45 NEUROLOGY 1873 (1995).

neurons are] destroyed, the patient will have numbness, severe inability to move and to coordinate movements, a phenomenon we call sensory ataxia . . .." Tr. 63:11–16. He cited to a paper by Dalmau et al., which found that this "was the presenting sign in 59% of patients, the primary problem in 62% of patients, and present eventually in 74% of patients." *Id.* (citing Resp't's Ex. C, tab 6).[35]

Dr. Lancaster opined that Ms. Garlanger's correct diagnosis was "paraneoplastic sensory neuropathy due to lung cancer." Tr. 60:11–14. During his testimony, Dr. Lancaster provided five main reasons why he did not believe that Ms. Garlanger suffered from GBS. First, Dr. Lancaster stated that Ms. Garlanger "had a picture that over time became apparent as a sensory predominant neuropathy, which favors the [anti-]Hu syndrome over GBS." Tr. 82:9–11. Second, Dr. Lancaster testified that he reviewed the three EMG studies that Ms. Garlanger underwent during her disease course and concluded that "they're much more consistent with sensory neuropathy from an anti-Hu paraneoplastic syndrome . . . due to the relatively minor and equivocal motor findings and the severe devastating loss of sensory nerve fibers over time . . .." Tr. 90:3–11. He noted that the EMG findings showed "that there was ongoing damage to the sensory neurons beyond probably four weeks." Tr. 82:14–15. Third, Dr. Lancaster found it "quite important" that Ms. Garlanger "had no significant recovery documented by eight to nine months after onset when she passed away. That would be possible . . . with GBS, but quite unlikely, whereas for [anti-]Hu [syndrome], it would be entirely consistent." Tr. 82:19–24. Fourth, Dr. Lancaster noted that Ms. Garlanger had "a tumor that[was] a small cell lung cancer[,] which make the anti-Hu syndrome far more likely than it would be otherwise be and actually far more likely than GBS." Tr. 82:25–83:3. Fifth, Dr. Lancaster stated that Ms. Garlanger "had a sky high titer to Hu antibodies." Tr. 83:3–4. Dr. Lancaster summarized that, "[p]utting together all of these different factors, we are more than 99 percent confident that this would be the [anti-]Hu paraneoplastic syndrome and not GBS." Tr. 83:5–7.

In his third expert report, Dr. Lancaster wrote that "[t]he loss of [deep tendon] reflexes is not a unique property to GBS." Resp't's Ex. H at 1. He explained that "[a]ny disease process of the sensory neurons, the motor neurons, the neuromuscular junction (communication between motor neuron and muscle cells) or muscle could result in suppressed or absent reflexes." *Id.* He further explained that, because "[s]ensory neuronopathy involves the destruction of primary sensory neurons, including those that detect muscle stretch[,]" the "loss of reflexes is the general rule as the disease process becomes severe enough to impair function." *Id.*

Dr. Lancaster acknowledged that clinicians had originally diagnosed Ms. Garlanger with GBS, but testified that Dr. Ward, one of Ms. Garlanger's clinicians, "changed his mind about the cause" of Ms. Garlanger's neurological symptoms. Tr. 138:1–6. Dr. Lancaster stated that Dr. Ward's February 14, 2012 note, which included the impression "[q]uestion post-vaccination [GBS] treated with IVIg [in] December 2011[,]" was an "indicat[ion that Dr. Ward] is now questioning that initial diagnosis of GBS." Tr. 137:16–20. While not a full retraction, Dr. Lancaster explained that "doctors don't usually practice in terms of issuing retractions," and this note demonstrated that Dr. Ward's "final conclusion was that it was paraneoplastic sensory neuropathy." Tr. 136:17–25.

[35] Dalmau et al., *supra* note 33.

On cross-examination, Dr. Lancaster was asked whether "there's a possibility that [Ms.] Garlanger . . . was transferred or infused the anti-Hu antibody through the five-day course treatment of IVIg[.]" Tr. 129:22–25. Dr. Lancaster answered that, while "possible," "the precise answer is [that is is] incredibly and astronomically unlikely that the IVIg would account for [Ms. Garlanger's] sky high result." Tr. 130:16–19. Dr. Lancaster continued, "[t]he odds that [Ms. Garlanger] got this through her IVIg . . . would require that a large number of randomly selected blood donors, all coincidentally had very high titers of Hu antibodies . . .[, which is] as close to impossible as you're going to get in medicine." Tr. 131:5–11.

Dr. Lancaster disagreed with Dr. Steinman's proposition that Ms. Garlanger had both anti-Hu paraneoplastic syndrome and GBS. Dr. Lancaster explained that "it would be unlikely for anyone to have both [GBS and anti-Hu paraneoplastic syndrome] at the same time." Resp't's Ex. E at 4. He explained that the GBS incidence rate is "[one]-[two] cases per 100,000 per year[,]" while "[t]he incidence of the anti-Hu paraneoplastic syndrome is much rarer, probably less than [one] patient per million per year." *Id.* Dr. Lancaster also noted that "this theory would predict that the GBS component of [Ms. Garlanger's] injury would show substantial recovery after nine months." *Id.* at 4–5. However, Dr. Lancaster opined that "[t]he lack of any significant recovery supports the theory that the nerve injuries were due entirely to anti-Hu." *Id.* at 5.

Dr. Lancaster disputed Dr. Steinman's assertion that there are cases of GBS caused by anti-Hu antibodies because "the anti-Hu paraneoplastic syndrome is a clinically and immunologically . . . different disease than GBS." *Id.* at 2. Dr. Lancaster provided the following table listing the differences between GBS and anti-Hu paraneoplastic syndrome:

Feature	**Anti-Hu**	**GBS**
Pathogenesis	Cytotoxic T-cell response targeting neuron	Demyelination of peripheral nerves due to autoantibodies to peripheral nerve gangliosides and/or proteins
Antigens	The Hu proteins deep inside neurons (The main one is called "HuD")	Gangliosides and peripheral nerve membrane proteins
Lab Testing	Hu antibody test (also called ANNA-1), particularly at very high titers as in the present case	Ganglioside antibody tests, various peripheral nerve protein antigens reported in numerous research studies
Symptoms	Typically progress over more than [four] weeks. Usually sensory-predominant. Lack of recovery. All consistent with the present case	Generally has significant motor component. Peaks within [two]-[three] weeks

Electrophysiology	Loss of sensory responses, mild diffuse slowing of sensory and motor responses, milder motor abnormalities. Consistent with the present case	Severe slowing and/or conduction block by multifocal demyelination
Triggering Events	Tumors, particularly small cell lung cancers in 77.5% (as in the present case)	Various infections such as campylobacter
Mechanism of Recovery	Sensory neurons cannot be replaced – none	Remyelination of sensory or motor fibers. And, for motor fibers only, collateral sprouting
Outcomes	Poor. Usually no recovery as in the present case	Substantial improvement over weeks to months is the norm

Id. at 3–4.

Dr. Lancaster also disagreed with Dr. Steinman's assertion that the flu vaccine worsened Ms. Garlanger's paraneoplastic syndrome. *Id.* Dr. Lancaster wrote that "[t]here is no evidence that vaccination can affect the anti-Hu paraneoplastic response." *Id.* Dr. Lancaster noted that "[t]here is no known homology between any component of the [flu] vaccine and the Hu proteins." *Id.*

IV. Applicable Legal Standard

To receive compensation under the Vaccine Act, Petitioner must demonstrate either that: (1) she suffered a "Table Injury" – i.e., an injury falling within the Vaccine Injury Table – corresponding to the vaccine in question within the time frame prescribed by the Vaccine Injury Table set forth at § 14, as amended by 42 C.F.R. § 100.3; or (2) that her illness is an "off-Table Injury," one not listed on the Table, that resulted from her receipt of a covered vaccine. *See* § 11(c)(1)(C); *Moberly v. Sec'y of Health & Human Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Capizzano v. Sec'y of Health & Human Servs.*, 440 F.3d 1317, 1319–20 (Fed. Cir. 2006). Petitioner does not assert a Table claim. Thus, she must prove that Ms. Garlanger's vaccine was the cause-in-fact of her injury.

To establish causation-in-fact, Petitioner must demonstrate by a preponderance of the evidence that the vaccine was the cause of Ms. Garlanger's injury. § 13(a)(1)(A). That is, a petitioner must offer evidence that leads the "trier of fact to believe that the existence of a fact is more probable than its nonexistence before [she] may find in favor of the party who has the burden to persuade the judge of the fact's existence." *Moberly*, 592 F.3d at 1322 n.2; *see also Snowbank Enter. v. United States*, 6 Cl. Ct. 476, 486 (1984) (mere conjecture or speculation is insufficient under a preponderance standard). Proof of medical certainty is not required. *Bunting v. Sec'y of*

Health & Human Servs., 931 F.2d 867, 873 (Fed. Cir. 1991). Petitioner must demonstrate that the vaccine was "'not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury.'" *Moberly*, 592 F.3d at 1321–22 (quoting *Shyface v. Sec'y of Health & Human Servs.*, 165 F.3d 1344, 1352–53 (Fed. Cir. 1999)). The vaccine received, however, need not be the predominant cause of the injury. *Shyface*, 165 F.3d at 1351.

In the seminal case of *Althen v. Sec'y of Health and Human Servs.*, the Federal Circuit set forth a three-pronged test used to determine whether a petitioner has established a causal link between a vaccine and the claimed injury. *See* 418 F.3d 1274, 1278–79 (Fed. Cir. 2005). The *Althen* test requires a petitioner to set forth: "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." *Id.* at 1278. To establish entitlement to compensation under the Program, petitioners are required to establish each of the three prongs of *Althen* by a preponderance of the evidence. *See id.*

Specifically, under the first prong of *Althen*, a petitioner must offer a scientific or medical theory that answers in the affirmative the question "can the vaccine(s) at issue cause the type of injury alleged?" *See Pafford v. Sec'y of Health & Human Servs.*, No. 01-0165V, 2004 WL 1717359, at *4 (Fed. Cl. Spec. Mstr. July 16, 2004), *mot. for rev. den'd*, 64 Fed. Cl. 19 (2005), *aff'd*, 451 F.3d 1352 (Fed. Cir. 2006). To satisfy this prong, a petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994); *see also Boatmon v. Sec'y of Health and Human Servs.*, 941 F.3d 1351, 1359 (Fed. Cir. 2019). Such a theory must only be "legally probable, not medically or scientifically certain." *Id.* at 548–49.

In addition to showing that the vaccine at issue can cause a particular injury, a petitioner must also, under *Althen's* second prong, prove that the vaccine actually did cause the alleged injury in her particular case. *See Pafford*, 2004 WL 1717359, at *4; *Althen*, 418 F.3d at 1278. A petitioner does not meet this obligation by showing only a temporal association between the vaccination and the injury; the petitioner "must explain *how* and *why* the injury occurred." *Pafford*, 2004 WL 1717359, at *4 (emphasis in original) (internal citations omitted). Ruling out other potential causes is an important element but does not itself establish causation. *Id.* Additionally, conjecture or speculation does not meet the preponderance standard. *Id.*

Although a temporal association alone is insufficient to establish causation, under the third prong of *Althen*, a petitioner must show that the timing of the injury fits with the causal theory. *See Althen*, 418 F.3d at 1278. The special master cannot infer causation from temporal proximity alone. *See Thibaudeau v. Sec'y of Health & Human Servs.*, 24 Cl. Ct. 400, 403–04 (Fed. Cl. 1991); *see also Grant*, 956 F.2d at 1148 ("'[T]he inoculation is not the cause of every event that occurs within the ten[-]day period. . . . Without more, this proximate temporal relationship will not support a finding of causation.'" (quoting *Hasler v. United States*, 718 F.2d 202, 205 (6th Cir. 1983))). A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *de Bazan v. Sec'y of Health & Human Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must also coincide with the

theory of how the relevant vaccine can cause an injury (Althen prong one's requirement). *Id.* at 1352; *Shapiro v. Sec'y of Health & Human Servs.*, 101 Fed. Cl. 532, 542 (2011), *recons. den'd after remand*, 105 Fed. Cl. 353 (2012), *aff'd mem.*, 503 Fed. App'x 952 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Human Servs.*, No. 11-355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for review den'd* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

Alternatively, a petitioner may be able to establish entitlement by showing that the vaccine at issue significantly aggravated a pre-existing condition. The Vaccine Act defines significant aggravation as "any change for the worse in a pre[-]existing condition which results in markedly greater disability, pain, or illness accompanied by substantial deterioration of health." § 300aa-33(4). When a petitioner makes this argument, the evidentiary burden is expanded. *See Loving v. Sec'y of Health and Human Servs.*, 86 Fed. Cl. 135, 144 (2009). In *Loving*, the Court set forth a six-factor test, which requires petitioners to establish each of the following by a preponderance of the evidence:

> (1) the person's condition prior to administration of the vaccine, (2) the person's current condition (or the condition following the vaccination if that is also pertinent), (3) whether the person's current condition constitutes a "significant aggravation" of the person's condition prior to vaccination, (4) a medical theory causally connecting such a significantly worsened condition to the vaccination, (5) a logical sequence of cause and effect showing that the vaccination was the reason for the significant aggravation, and (6) a showing of a proximate temporal relationship between the vaccination and the significant aggravation.

Id.

The *Loving* analysis requires the special master to "evaluat[e] whether the vaccine made the person worse than the person would have been but for the vaccination. In doing so, the natural course of the disease must be considered." *Locane v. Sec'y of Health & Human Servs.*, No. 99-589V, 2011 WL 3855486 at *10 (Fed. Cl. Spec. Mstr. Feb. 17, 2011), *mot. for review den'd*, 99 Fed. Cl. 715 (2011), *aff'd*, 685 F.3d 1375 (Fed. Cir. 2012); *see also Hennessey v. Sec'y of Health & Human Serv.*, No. 01-190V, 2009 WL 1709053, at *41-42 (Fed. Cl. Spec. Mstr. May 29, 2009), *mot. for review den'd*, 91 Fed. Cl. 126 (2010).

Respondent frequently offers experts to rebut a petitioner's case. Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen v. Sec'y of Health & Human Servs.*, 618 F.3d 1339, 1347 (Fed. Cir. 2010) (internal citations omitted). Weighing the relative persuasiveness of competing expert testimony, based on a particular expert's credibility, is part of the overall reliability analysis to which special masters must subject expert testimony in Vaccine Program cases. *Moberly*, 592 F.3d at 1325–26 ("[a]ssessments as to the reliability of expert testimony often turn on credibility determinations"); *see also Porter v. Sec'y of Health & Human Servs.*, 663 F.3d 1242, 1250 (Fed. Cir. 2011) ("this court has unambiguously explained that special masters are expected to consider the credibility of expert witnesses in evaluating petitions for compensation under the Vaccine Act").

Under the Vaccine Act, petitioners are not entitled to compensation if the special master finds by a preponderance of the evidence "that the illness, disability, injury, condition, or death described in the petition is due to factors unrelated to the administration of the vaccine described in the petition." § 300aa-13(1)(B). However, petitioners who satisfy *Althen* are entitled to compensation, unless Respondent can demonstrate by a preponderance of the evidence that the injury was caused by factors unrelated to the vaccination. *See Althen*, 418 F.3d at 1278; *Paluck v. Sec'y of Health & Human Servs.*, 786 F.3d 1373, 1386 (Fed. Cir. 2015) (citing *de Bazan v. Sec'y of Health & Human Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008) (holding that it is not a petitioner's burden "to rule out possible alternative causes" (internal citations omitted))); *Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 547 (Fed. Cir. 1994). When an injury is in dispute, the special master may "determine which injury [is] best supported by the evidence presented in the record before applying the Althen test so that the special master could subsequently determine causation relative to the injury." *Broekelschen*, 618 F.3d at 1346; *see also Lombardi v. Sec'y of Health and Human Servs.*, 656 F.3d 1343, 1353 (Fed. Cir. 2011) (finding that "it was appropriate for the special master to first determine what injury, if any, was supported by the evidence presented in the record before applying the *Althen* test to determine causation.").

Both parties filed medical and scientific literature in this case, but not every filed item was probative to the outcome of this decision. While I have reviewed all of the medical literature submitted in this case, I discuss only those articles that are most relevant to my determination and/or are central to Petitioner's case – just as I have not exhaustively discussed every individual medical record filed. *Moriarty v. Sec'y of Health & Human Servs.*, 844 F.3d 1322, 1328 (Fed. Cir. Apr. 6, 2016) ("[w]e generally presume that a special master considered the relevant record evidence even though he does not explicitly reference such evidence in his decision") (citation omitted); *see also Paterek v. Sec'y of Health & Human Servs.*, 527 Fed. App'x 875, 884 (Fed. Cir. 2013) ("[f]inding certain information not relevant does not lead to – and likely undermines – the conclusion that it was not considered").

V. Analysis

A. Clinical Presentation

Ms. Garlanger's initial presentation of back and right lower side pain occurred approximately two weeks post vaccination, but her physicians did not identify her condition as neurological in nature or related to her vaccination. A few days later, she complained of tingling, and her symptoms expanded to include her arm, but an unremarkable neurological examination did not reveal evidence of neuropathy. As Ms. Garlanger's symptoms continued to worsen, treating physicians began to consider loss of neurological function, including stroke, and conducted additional testing for signs of neuropathy. Post testing, it was clear from her CSF and positive antibody levels that Ms. Garlanger's condition was neurological, and her treating neurologist concluded that her presentation was most consistent with "an acute inflammatory demyelinating polyneuropathy [that] may be secondary to her vaccine exposure."[36] Pet'r's Ex. 3 at 4.

[36] GBS is a type of acute inflammatory demyelinating polyneuropathy, and Ms. Garlanger's medical history reflects that this diagnosis by Dr. Ward was later referred to as GBS and treated as such.

Petitioner would have the analysis end there and attribute any additional findings to a wholly separate clinical course that developed simultaneously. Indeed, Petitioner argues that "respondent's expert is the only such individual to suggest that the *only* condition [Ms. Garlanger] had was a small cell carcinoma and paraneoplastic syndrome." Pet'r's Post-Hr'g Br. at 2 (emphasis in original). This is not accurate. Ms. Garlanger was initially diagnosed by Dr. Ward in December of 2011. In a follow up on January 6, 2012, he maintained that she had a "demyelinating polyneuropathy with secondary axonal degeneration[,] although he noted "no evidence of ongoing acute denervation." Pet'r's Ex. 3 at 18. Approximately one week later, Dr. DilanSzanto noted in a medical record dated January 13, 2012, "[w]ith the inflammatory demyelination, lung nodule, [and] SIADH, consideration from GBS *would now shift* to the etiology of paraneoplastic syndrome most possibly small cell CA." Pet'r's Ex. 11 at 505. Impressions from that visit include: lung nodule, SIADH, generalized inflammatory demyelinating polyneuropathy, neurogenic bladder, dyslipidemia, and history of seizure. *Id.* Dr. DilanSzanto had additional information that was not available to Dr. Ward at the time of his diagnosis, and she articulated that these additional factors changed Ms. Garlanger's diagnosis. Dr. DilanSzanto did not include GBS as a differential diagnosis in her impressions, and she followed up on January 14, 2012, concluding that "[t]he most likely diagnosis is a small cell lung carcinoma with a paraneoplastic syndrome, i.e., SIADH." Pet'r's Ex. 11 at 510. That pattern continued. "Myopathy may be a paraneoplastic manifestation rather than GBS." *Id.* at 602. And Dr. Ward's impressions as of February 14, 2012, were "[p]redominantly sensory neuronopathy consistent with paraneoplastic process." Pet'r's Ex. 5 at 46. He referred to the post-vaccination GBS as "questionable" and discussed Dr. Rezania's opinion that "this might be paraneoplastic syndrome in light of the lung nodule and the SIADH that was present." *Id.* Dr. Ward seems to also consider that this diagnosis is more accurate with the additional information. Ms. Garlanger's complete medical history provides preponderant evidence that although GBS was identified as an initial diagnosis, her treaters shifted away from that condition after additional testing was completed.

B. Diagnosis

Due to Ms. Garlanger's rapid deterioration following the discovery of lung cancer, her treaters never definitively diagnosed her neurological condition. The death certificate lists paraneoplastic syndrome with GBS as a significant condition, but it is unclear if these should be considered as one disease, e.g., an umbrella condition with a subtype, or two separate conditions.

Dr. Steinman argued that Dr. DilanSzanto's diagnosis was only a suggestion, but later conceded that there was sufficient medical evidence to support her opinion. Dr. Steinman's refusal to assert a clear position clouds his argument. On the one hand, Dr. Steinman argued that the small cell carcinoma diagnosis was inferential when compared to the definitive vaccination, and therefore, any subsequent neuropathy should be attributed to the vaccination, an established occurrence. On the other hand, he ultimately conceded that he could not say that Ms. Garlanger's SIADH is associated with GBS "just as much" as it is with small cell carcinoma. He argued that the type of cancer that Ms. Garlanger developed was inconsequential despite the argument and supporting medical literature that Dr. Lancaster provided to show a correlation between SIADH, paraneoplastic syndrome, and small cell carcinoma. Dr. Steinman also agreed with this correlation in his own article wherein he wrote, "paraneoplastic diseases involve neuronal autoimmunity due

to a tumor antigen, often intercellular, that is shared with the nervous system." Pet'r's Ex. 18 at 2.

Respondent's expert, Dr. Vargas, based her opinion that Ms. Garlanger suffered from paraneoplastic syndrome on Ms. Garlanger's presentation, including her sensory and motor neuropathy, ataxia, autonomic dysfunction, possible lower motor neuron disease, and syndrome of inappropriate secretion of anti-diuretic hormone." Rep't's Ex. A at 8. Dr. Vargas clearly explained that while some of these symptoms are seen in GBS, Ms. Garlanger's complete workup is better captured by paraneoplastic syndrome. I find this consistent with Ms. Garlanger's diagnosis evolving as more of her symptoms were discovered. Dr. Vargas also noted that GBS can a be a manifestation of paraneoplastic syndrome. All of the experts agreed that paraneoplastic syndromes are neurological problems associated with cancer. Dr. Vargas clearly explained how a neuropathy that first presented as GBS in the absence of any indication of cancer would in fact be paraneoplastic syndrome when cancer was confirmed.

Dr. Lancaster also argued that Ms. Garlanger suffered from paraneoplastic sensory neuropathy due to lung cancer. In direct contrast to Dr. Steinman, Dr. Lancaster was consistent in his opinion throughout his written reports and testimony. Furthermore, his chart explained how paraneoplastic syndromes are linked to cancer patients and differ in their manifestation when compared to GBS. Dr. Lancaster also provided medical literature to support his assertion that paraneoplastic syndrome was a much more likely scenario than one wherein a patient was simultaneously suffering from GBS, cancer, and paraneoplastic syndrome. He discussed Dr. Ward's note of a question of the post-vaccination GBS and admitted that doctors do not commonly offer full retractions. The evidence provided by Ms. Garlanger's treaters, Petitioner's experts, and Respondent's experts establish it is more likely than not that Ms. Garlanger suffered from paraneoplastic syndrome. Petitioner did not present preponderant evidence that Ms. Garlanger's treaters ultimately concluded that she also suffered from GBS.

C. Causation

Petitioner alleged in her initial filing and subsequent briefings that Ms. Garlanger developed a flu vaccine-induced GBS via molecular mimicry. This pathogenic process is well documented in the Vaccine Program, and Dr. Steinman provided medical literature and discussion in his expert reports and testimony as corroboration. The fact that GBS can be caused by the flu vaccine via molecular mimicry is not in dispute here and not relevant to this case. Ms. Garlanger's history does not sufficiently support that diagnosis, and Ms. Garlanger's carcinoma would preclude any causation theory that ignores this condition.

Eventually, even Dr. Steinman expanded his opinion from "a high degree of medical certainty that the influenza vaccine on Oct 15, 2011[,] triggered [Ms. Garlanger's] GBS," Pet'r's Ex. 12 at 15, to "the immunization would have been the aggravating factor that ended decades of dormancy of her disease, only to become manifest weeks after immunization[,]"[37] Pet'r's Ex. 28 at 7. He did not clarify in his report what he meant by 'decades of dormancy of her disease.'

[37] Dr. Steinman did not mention molecular mimicry in this modified theory based on what appears to be significant aggravation.

During his testimony, Dr. Steinman stated that Ms. Garlanger "had the cancer for a long time." Tr. 54:15–18. When he was asked what manifested weeks after immunization, he stated GBS, but also stated "the aggravation was the emergence of the syndrome that's associated with cancer." Tr. 55:23–56-:2. Dr. Steinman seemed to opine that GBS is a manifestation of a paraneoplastic syndrome in someone that already has cancer and is then vaccinated. However, this is inconsistent with his assertion that Ms. Garlanger had both GBS and paraneoplastic syndrome. Dr. Steinman testified that "the Venn diagram of GBS and paraneoplastic syndrome overlap. So . . . I'm trying to reconcile two balls in the air." Tr. 54:23–25. Dr. Steinman was unable to state unequivocally whether Ms. Garlanger had a paraneoplastic syndrome and GBS simultaneously, or if her GBS was a manifestation of her paraneoplastic syndrome. Ultimately, I am unable to identify a coherent scientific or medical theory to explain how the flu vaccine caused Ms. Garlanger's neuropathy, because Dr. Steinman did not articulate one. Furthermore, Petitioner's briefing does not even mention that Petitioner's treaters explicitly shift from GBS to SIADH, which her treaters characterize as a manifestation of her paraneoplastic syndrome. Dr. Steinman was forced to confront this reality in the medical records, and he did not oversimplify his discussion of Ms. Garlanger's condition in the same vein as Petitioner's briefings.

There is overwhelming literature that explains flu vaccine-induced GBS; however, Petitioner's own expert conceded that this mechanism is too simple to begin to explain what occurred in a case like Ms. Garlanger's. Therefore, I do not find that Petitioner presented preponderant evidence that Petitioner developed flu vaccine-induced GBS, cancer notwithstanding. Furthermore, Petitioner did not present a biological mechanism whereby Ms. Garlanger's flu vaccine, to quote Dr. Steinman, "ended decades of dormancy of her disease, only to become manifest weeks after immunization," Pet'r's Ex. 28 at 7, as GBS, which was the "emergence of the syndrome that is associated with cancer," Tr. 55:23–56:2.

Dr. Steinman's brief reference to the flu vaccine as a significant aggravator is not supported by any documentation in the medical records that Ms. Garlanger's condition was expedited or worsened due to vaccination. Dr. Steinman did not rely on any event in Ms. Garlanger's history, medical literature, or even a single case study, to illustrate how vaccination could or did play a role in the worsening of her paraneoplastic syndrome. On the other hand, Dr. Vargas was very detailed in her explanation of the development of Ms. Garlanger's paraneoplastic syndrome. As previously established, there was nothing to suggest that her course was aggravated in any way. Likewise, Dr. Lancaster also clearly articulated how Ms. Garlanger's condition and all her symptoms can be explained by her paraneoplastic syndrome and small cell carcinoma. Dr. Lancaster's reliance on Petitioner's neuronopathy diagnosis is also supported by the medical reference indication that neuronopathy is commonly associated with small cell carcinoma. Indeed, despite Ms. Garlanger's smoking history, Respondent's experts did not focus on that potentially aggravating factor to explain pathogenesis. After a consideration of the record, there has not been preponderant evidence presented to show that the flu vaccine made Ms. Garlanger worse than she would have been but for the vaccination.

I also note that while Respondent has no obligation to present an alternative cause unless and until Petitioner has presented preponderant evidence of a sound and reliable causation theory, Respondent's rebuttal to Petitioner's expert provided a more likely explanation of the relationship between carcinoma, cancer-related disease, and neuropathy, vaccination notwithstanding. I will

not conduct an alternative causation analysis here, because Petitioner did not establish a prima facie case of causation to trigger Respondent's burden to provide preponderant evidence that Ms. Garlanger's injuries were caused by something other than vaccination.

D. Timing

The medical records in this case illustrate that Ms. Garlanger's initial symptoms occurred within one month of vaccination. That time frame would be an appropriate temporal relationship for flu vaccine-induced GBS. Respondent notes that Ms. Garlanger's condition began with an atypical presentation of back pain and muscle spasms that had started to improve when, approximately six weeks post vaccination, she developed additional symptoms of weakness and incoordination. Ms. Garlanger's treaters diagnosed her with GBS subsequent to the development of these additional symptoms, but prior to the discovery of her carcinoma. If the time frame is adjusted in consideration of Ms. Garlanger's additional symptoms, six weeks could also be appropriate for GBS or a more general vaccine-induced neuropathy.

The appropriateness of the temporal relationship is of no consequence in this case, however, because I do not find that Petitioner presented preponderant evidence that Ms. Garlanger suffered from flu-induced GBS as alleged in the petition. Rather, a paraneoplastic syndrome was the more likely cause of Ms. Garlanger's symptoms, and Petitioner did not present an appropriate time frame to consider for the development of GBS in conjunction with a paraneoplastic syndrome after a pre-existing cancer is aggravated due to vaccination. Therefore, I do not find that *Althen* prong three can be applied to Ms. Garlanger's presentation, and Petitioner has not met her burden.

VI. Conclusion

After a review of the record, including Ms. Garlanger's medical records, expert reports, accompanying literature, and testimony, Petitioner has not proven it more likely than not that Ms. Garlanger suffered from GBS, vaccine-induced or otherwise. Petitioner's expert was unable to articulate a clear injury or a causation theory applicable Ms. Garlanger's specific medical history. Petitioner failed to establish it was more likely than not that Ms. Garlanger's influenza vaccination caused the development of GBS, significantly aggravated her cancer, and/or led to a paraneoplastic syndrome. Therefore, Petitioner has not satisfied her burden under *Althen*. It is unquestionable that Petitioner has suffered immense loss and understandable that she would seek out answers on behalf of Ms. Garlanger. I have reviewed the entire record in order to make an informed determination whether Mrs. Garlanger's neuropathy was a result of her vaccination. I could not conclude that it was. Petitioner's claim is hereby **DENIED**.

In the absence of a timely-filed motion for review filed pursuant to Vaccine Rule 23, **the Clerk of the Court is directed to ENTER JUDGMENT** consistent with this decision.[38]

IT IS SO ORDERED.

s/Herbrina D. Sanders
Herbrina D. Sanders
Special Master

[38] Pursuant to Vaccine Rule 11(a), entry of judgment is expedited by the parties' joint filing of a notice renouncing the right to seek review.